REMARKS

Reconsideration of this application is requested in view of the amendments to the claims and the remarks presented herein.

The claims in the application are claims 20 to 28, all other claims having been cancelled.

Applicants are submitting herewith a substitute specification which incorporates SEQ ID No: 10 and SEQ ID No: 11 therein and new pages 6, 10, 13 and 14 of the specification are also enclosed herewith. Applicants are also enclosing a new paper copy of the sequence listing and a computer readable diskette containing the same. The paper copy of the compact disk of the sequence listing are the same and where applicable, include no new matter as required by 37 CFR 1.821(e), 1.821(f), 1.821(g), 1.825(b) or 1.825(d). The new specification does not include any new matter.

Claims 12 to 14 were rejected under 35 USC 112, second paragraph, as being indefinite since the Examiner was of the opinion that claims 12 and 14 were of the same scope. Claim 13 was objected to in the expression "several tens of μm" and claims 12 and 14 were objected to according to "the suppression of an amino acid".

Applicants respectfully traverse these grounds of rejection since the new claims are deemed to clearly comply with 35 USC 112. With respect to claims 12 and 14 which have been replaced with claims 20 and 25, it is deemed that they are of different scope. Claim 20 is drawn to a pharmaceutical composition containing starch granules containing at least one fusion polypeptide while claims 14 and 25 now presented, relate to the pharmaceutical composition containing at least one fusion polypeptide. In other words, claim 20 is directed to a composition comprising a starch granule while claim 25 does not. Therefore, the new claims are believed to comply with 35 USC 112 and withdrawal of this rejection is requested.

Claims 12 to 14 were rejected under 35 USC 112, first paragraph, since the Examiner was of the opinion that the specification was not enabling for claims of this scope since the claims included a fusion protein comprising any variant thereof. They were also directed to starch synthases and variations thereof which were not supported by the specification.

Applicants respectfully traverse these grounds of rejection since it is deemed that the specification is enabling for the claims of the present scope which are directed to pharmaceutical compositions containing starch granules comprising fusion polypeptides between a polypeptide of interest and the granule bound starch synthase GBSSI of *Chlamydomonas reinhardtii* or fragments thereof which is clearly supported by the

application and to pharmaceutical compositions containing said fusion polypeptides. Therefore, the present claims are clearly enabled by the specification and withdrawal of these grounds of rejection is requested.

Claims 12 to 14 were rejected under 35 USC 102 as being anticipated by or under 35 USC 103 as being obvious over the Keeling et al reference. The Examiner states that the reference discloses "starch encapsulated protein" comprising a fusion protein consisting of a starch synthase capable of binding to starch granule or migrate to the site of starch granule biosynthesis fused through its C-terminal to a heterologous peptide or polypeptide. The Examiner concedes that the reference does not disclose pharmaceutical compositions for Applicants' starch granule and the proportion of starch by weight but the composition of the reference inherently has the said dimensions and percent by weight or it would have been obvious to amend the same.

Applicants respectfully traverse this ground of rejection since it is not deemed that the Keeling et al reference anticipates or renders obvious Applicant's invention. The Keeling et al reference relates to a hybrid polypeptide comprising a starch encapsulating region (SER) from a starch binding enzyme and a polypeptide of interest fused to said SER wherein the polypeptide of interest can be a biologically active polypeptide. The expression "SER" used in the reference is vague and indefinite and does not teach one skilled in the art anything.

Lines 14 to 27 of page 13 of the reference mentions that the SER is the region of the subject polypeptide that has a binding affinity for starch and that the SER is selected from the group of peptides comprising SER of starch synthases and branching enzymes of plants, along which specific enzymes starch synthase (STS), granule bound starch synthase (GBSTS) and branching enzymes (BE) of starch bearing plants. It is also stated in lines 23 to 26 of page 21 that the SER can be elucidated using site-directed mutagenesis and other genetic engineering methods known to one skilled in the art.

From line 28 of page 25 through line 3 of page 26 of the reference, it is mentioned that the SER region is located closer to the C-terminus end than the N-terminus end of the starch synthesizing genes or starch binding genes such as genes fro amylases. If some SER regions have been elucidated in the prior art in the case of some soluble starch-syntheses and amylases of plants, no SER regions have been found for the time being in the case of the granule bound starch-synthases.

It is specified in lines 24 to 26of page 16 of the reference that the gene sequence for the payload polypeptide is preferably attached at the N-terminus end of the SER sequence. The examples of starch-synthase genes used in this document are the following:

1) the waxy (i.e. GBSS) gene in maize and rice, 2) the soluble starch synthase I, Ia and IIb genes in maize and 3) the maize branching enzymes I and II genes.

The reference only refers to the use of starch synthase of plants but does not mention the possible use of starch synthase from other sources and plants. Therefore, the document in no way relates to Applicants' granule bound starch synthase GBSSI from the micro-algae *Chlamydomonas reinhardtii* and fragments thereof as in the present claims and has no relationship to Applicants' pharmaceutical compositions containing said GBSSI or fragments thereof linked to a polypeptide of interest as in Applicants' claims.

Keeling et al would in no way teach a GBSSI isolated from *Chlamydomonas reinhardtii* or that the said GBSSI therefrom is at least 10 fold more active than the most active plant corresponding enzymes when the specific activities (activity v. amount of starch) were measured in comparison with potato, cassava, taro and wheat. (See for example the chapter Discussion on page 3817 of Wattebled et al, Eur. J. Biochem., Vol. 269 (2002) pp, 3810-3820).

In contrast to the Keeling et al teaching, it is clearly stated in the present application that the polypeptide of interest must be placed at the C-terminal end of the GBSSI or fragments thereof and not at the N-terminal end as described by Keeling et al.

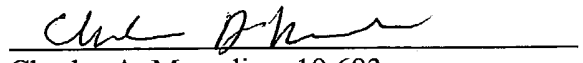
Applicants have found that the GBSSI of *Chlamydomonas reinhardtii* or a fragment thereof lacking the C-terminal end of approximately 16 kDa (i.e. the fragment

of 438 amino acids corresponding to SEQ ID No: 7) are able to bind to the starch granules. Therefore, the N-terminal end of the GBSSI is an important region for the binding to the starch granule and must not be modified by the presence of a polypeptide of interest for the binding to the starch granule and must not be modified by the presence of a polypeptide of interest which must be situated at the C-terminal end of the said GBSSI or fragments thereof lacking its C-terminal end.

To the contrary, Keeling et al teaches that the SER used in the fusion polypeptides has to correspond to a truncated starch synthase wherein the N-terminal end is deleted because Keeling et al supposed that the SER is located closer to the C-terminus end than the N-terminus end as mentioned above. Therefore, it would not be obvious to one skilled in the art from Keeling et al that the GBSSI is much more active than the GBSSI from plants and that the polypeptide of interest in pharmaceutical compositions as defined in Applicants' claims must be placed at the C-terminal end of the GBSSI or at the C-terminal end of fragments thereof lacking their C-terminal end as defined in Applicants' claims. Therefore, the reference neither anticipates nor renders obvious Applicants' invention and withdrawal of this ground of rejection is requested.

In view of the amendments to the claims and the above remarks, it is believed that the claims clearly point out Applicants' patentable contribution and favorable reconsideration of the application is requested.

Respectfully submitted,
Muserlian, Lucas and Mercanti



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Enclosures